Synthesis of Oxazocenones via Gold(I)-Catalyzed 8-Endo-Dig Hydroalkoxylation of Alkynamides

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Synthesis of Oxazocenones via Gold(I)-Catalyzed 8-*Endo*-Dig Hydroalkoxylation of Alkynamides

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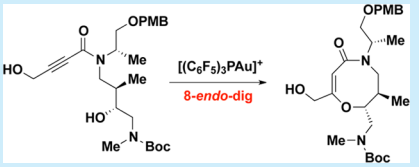
Supporting Information

ABSTRACT: Several benzoxazocenones have been found to exhibit novel cellular activities. In the present study, we report a gold(I)-catalyzed 8-*endo*-dig hydroalkoxylation reaction of alkynamides to access analogous oxazocenone scaffolds. This methodology provided an advanced intermediate, which was elaborated to a des-benzo analog of a bioactive benzoxazocenone.



Several benzoxazocenones (e.g., **1**–**4**, Figure 1)[1] having novel cellular activities have been discovered using cell-based screening of compounds prepared using diversity-oriented synthesis (DOS).[2,3] Of particular relevance to this study, BRD0476 (**3**)[1a] and quinoline analog BRD1116 (**4**)[1b] rescued INS-1E pancreatic β-cells from cytokine-induced apoptosis for the potential treatment of type-1 diabetes. Mechanism-of-action studies revealed **3** and **4** inhibit the JAK-STAT signaling pathway induced by pro-inflammatory cytokine IFN-γ.[1b]

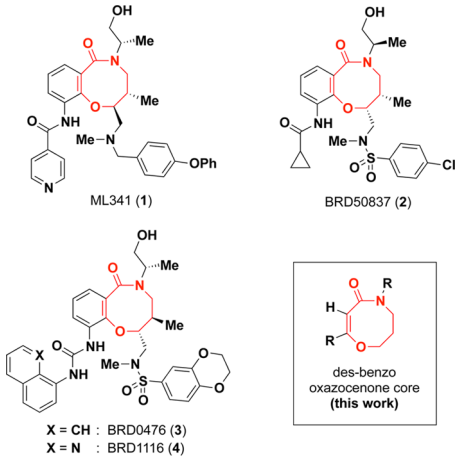
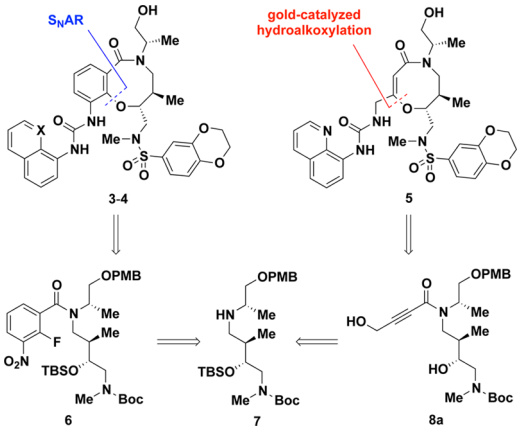


Figure 1. DOS-generated bioactive benzoxazocenones (**1**–**4**) and targeted des-benzo framework.

In an effort to optimize these promising activities, numerous analogs of **3** and **4** have been prepared, but structural modifications have been limited to appending *N*-alkyl side chain, urea, and sulfonamide moieties.[1a,b] In the present study, we describe a new synthesis of oxazocenones that lack a fused benzene moiety (des-benzo). The route enables the synthesis of analogs that possess changes in the cyclic core scaffold (Figure 1). Previously, the benzo-fused 8-membered ring in **3** and **4** was constructed using intramolecular nucleophilic aromatic substitution (S_NAR) of benzamide **6**, which was obtained from chiral amine building block **7** (Scheme 1).[1a,b,3] We envisioned that des-benzo congener **5** may also be derived from **7** via an analogous 8-*endo*-dig hydroalkoxylation reaction of alkynamide **8a**.[4,5]

Scheme 1. Retrosynthesis of Benzoxazocenones 3–4 and Oxazocenone 5 via Analogous Cyclization Pathways



Given that increased entropic and enthalpic barriers to cyclization are often associated with formation of medium rings,[6] we sought a robust method to prepare oxazocenones. Homogeneous gold catalysis has proven useful for synthetic transformations over the past few decades.[7] The ability of gold to serve as a carbophilic π Lewis acid to activate unsaturated C–C bonds renders these functionalities including alkynes susceptible to nucleophilic attack. However, there are relatively few examples of 8-*endo*-dig cyclizations catalyzed by gold, which include cycloisomerizations to indoloazocenes and benzoxocenes

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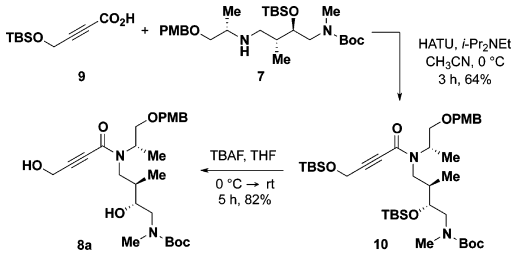
reported by the Echavarren[8] and Waldmann[9] laboratories, respectively. Hydroalkoxylation variants[10] to form 8-membered heterocycles have yet to be demonstrated, though gold(I) salts were serendipitously discovered by Van der Eycken et al. to catalyze an analogous 7-*endo*-dig hydroalkoxylation of an alkynamide.[10k] Here, we describe the extension of this methodology to the development of a gold(I)-catalyzed 8-*endo*-dig hydroalkoxylation to form oxazocenones en route to **5**.

We initiated our synthetic studies toward oxazocenone **5** from known 4-((*tert*-butyldimethylsilyl)oxy)-2-butynoic acid **9**[11] and chiral amine **7**[3] (Scheme 2). Acid **9** was chosen as a suitable

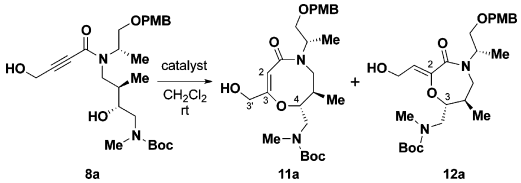
Scheme 2. Synthesis of Alkynamide 8a



building block to incorporate an alcohol as a functional group handle for installation of the urea moiety of **5** at a late stage in the synthesis (*vide infra*). Upon screening several reagents and conditions, we found that HATU-mediated amide coupling of **9** and **7** in MeCN at 0 °C provided alkynamide **10** in satisfactory yield (Scheme 2). Desilylation (TBAF) afforded deprotected substrate **8a** for evaluation of the gold(I)-catalyzed 8-*endo*-dig hydroalkoxylation reaction.

Intramolecular hydroalkoxylation of **8a** using catalytic Ph_3PAuCl (5 mol %) and $AgSbF_6$ (5 mol %) provided the desired 8-*endo*-dig oxazocenone product **11a** in CH_2Cl_2 at rt (entry 1, Table 1). In addition to **11a**, formation of oxazepanone **12a** was also observed under these conditions, likely resulting from a competitive 7-*exo*-dig cyclization. The ratio of products **11a** and **12a** was determined to be 1.7:1 by ^{1}H NMR analysis of the crude reaction mixture. Cyclization to these heterocycles was confirmed by key HMBC correlations between the C(3) and H(4) atoms as well as the C(2) and H(3) atoms for **11a** and **12a**, respectively. The products could be further distinguished by their NMR spectra. In particular, the signal in the ^{1}H NMR spectrum for the vinylic proton in **11a** existed as a singlet, whereas this signal in **12a** exhibited additional splitting due to the adjacent methylene group. Endocyclic olefins in 8-membered heterocycles can exist in both *E* and *Z* configurations.[9] A weak NOE signal was detected between the vinylic C(2) and methylene C(3′) protons in **11a**, suggesting preference for the *Z* geometry. Although no confirmatory NOE correlations were observed for oxazepanone **12a**, we expect that *anti*-addition of the alcohol to the alkyne, by analogy to the olefin geometry found in **11a**, would provide the exocyclic olefin in the *Z* configuration.

Table 1. Optimization for Selective Au(I)-Catalyzed 8-*Endo*-Dig Hydroalkoxylation to Oxazocenone 11a



entry	catalyst (5 mol %)	t^a (h)	ratio^b (**11**:**12**)	yield^c (%)
1	$Ph_3PAuCl/AgSbF_6$	30	1.7:1	88
2	$Ph_3PAuCl/AgOTf$	6	2.8:1	85
3	$(p\text{-}CF_3C_6H_4)_3PAuCl/AgOTf$	4.5	4.3:1	91 (74)^d
4	$(C_6F_5)_3PAuCl/AgOTf$	5	6.2:1	83 (77)^d
5	$(C_6F_5)_3PAuCl$	19	–	–^{e}
6	AgOTf	72	16.7:1	40^{f,g}
7	TfOH	25	–	–^{e}

^{a}Reactions were monitored by LCMS. ^{b}Product ratio determined by ^{1}H NMR analysis of the crude reaction mixture. ^{c}Combined isolated yields of **11a** and **12a** after column chromatography unless otherwise noted. ^{d}Isolated yield of **11a**. ^{e}Starting material was recovered. ^{f}Yield determined by ^{1}H NMR analysis using toluene as an internal standard. ^{g}Partial conversion of starting material was observed.

We next turned our attention to increasing the selectivity for formation of oxazocenone **11a**. Changing the silver additive to AgOTf increased the ratio to 2.8:1 (entry 2, Table 1). This result suggests that the gold complex generated *in situ* may have increased cationic character, activating the alkynamide for oxa-Michael addition by the alcohol and leading to shorter reaction times (entries 2−4). Tuning the ligand also enhanced the cationic character of the gold complex. For example, adding electronegative groups to the aryl moieties of phosphine ligands increased selectivities (entries 3 and 4), in which $(C_6F_5)_3PAuCl$[12] provided a 6.2:1 ratio to give an optimal yield (77%) for **11a** (entry 4). Although 5 mol % AgOTf alone catalyzed the reaction with high selectivity for **11a**,[13] low conversion and isolated yields were observed (entry 6).[14] Furthermore, $(C_6F_5)_3PAuCl$ or TfOH, which is often the active catalyst for reactions using metal triflates,[15] by itself did not provide conversion to **11a** or **12a** (entries 5 and 7, respectively). Taken together, these control experiments suggest that $(C_6F_5)_3PAu^+$ is the cationic species activating alkynamide **8a** for intramolecular hydroalkoxylation. Exemplifying the mildness and utility of this reaction, base-mediated cyclization to **11a** under dissociative anion conditions (e.g., KO*t*-Bu/18-crown-6 or *n*-BuLi/HMPA)[4a,b,d] was not achieved.

Having optimized conditions for a highly complex alkynamide, we next determined the generality and scope of the gold(I)-catalyzed hydroalkylation reaction to oxazocenones (Scheme 3). Surprisingly, simplified alkynamide **8b**, which lacks substituents on the *N*-alkyl groups but retains the propargylic alcohol, cyclized to oxazocenone **11b** without observation of the *exo* byproduct **12b**. On the other hand, TBS-protected alkynamide **8c** provided oxazocenone **11c** along with small amounts of 7-*exo*-dig product **12c** (11:1 *endo* to *exo* selectivity determined by ^{1}H NMR analysis of the crude reaction mixture). Other substitutions at the propargylic position provided selective formation of oxazocenones. For example, methyl- and phenyl-substituted oxazocenones **11d** and **11e** were synthesized in good yields at 79% and 84%, respectively. Alkynamides with various substituents (R_3) on the *N*-alkyl group bearing the nucleophilic alcohol were also tolerated for the reaction. Oxazocenones **11f** and **11g** with substitutions at the C(5)- and C(4)-positions, respectively, were selectively formed in good yields. Although a slower reaction time for conversion to **11f** (24 h) versus **11e** (6.5 h) seems counterintuitive, "reverse" *gem*-disubstitution effects have previously been shown for formation of medium rings.[16] Demonstrating that sterically hindered tertiary alcohols are suitable for cyclization, geminal dimethyl-substituted oxazocenone **11h** was prepared in moderate yield. Unfortunately, aryl substitution (R_2) of the amide produced **11i** in low yield (20%),

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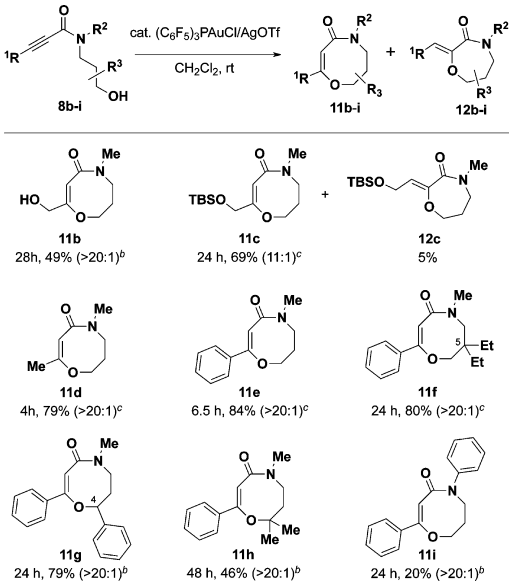
Scheme 3. Substrate Scope for Cyclization to Oxazocenones[a]

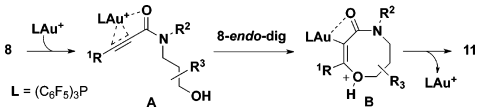


[a]Reaction times and isolated yields are given with ratios of **11** to **12** in parentheses. [b]Reaction was performed using 10 mol % $(C_6F_5)_3PAuCl$ and 10 mol % AgOTf. [c]Reaction was performed using 5 mol % $(C_6F_5)_3PAuCl$ and 5 mol % AgOTf.

demonstrating a limitation of this reaction. Poor yields were also observed for substrates containing a secondary amide or a terminal alkyne (not shown). The structural and olefin-geometry assignment of oxazocenones formed during the gold(I)-catalyzed cyclization were confirmed by the X-ray crystal structures of **11b**, **11e**, **11h**, and **11i**.

The mechanism accounting for selective 8-*endo*-dig cyclizations to oxazocenones may exploit dual π and σ Lewis acid properties[17] of $(C_6F_5)_3PAu^+$. Activation of the amide carbonyl with the Au(I) catalyst likely significantly promotes oxa-Michael addition in the hydroalkoxylation reaction of **8** (Scheme 4).

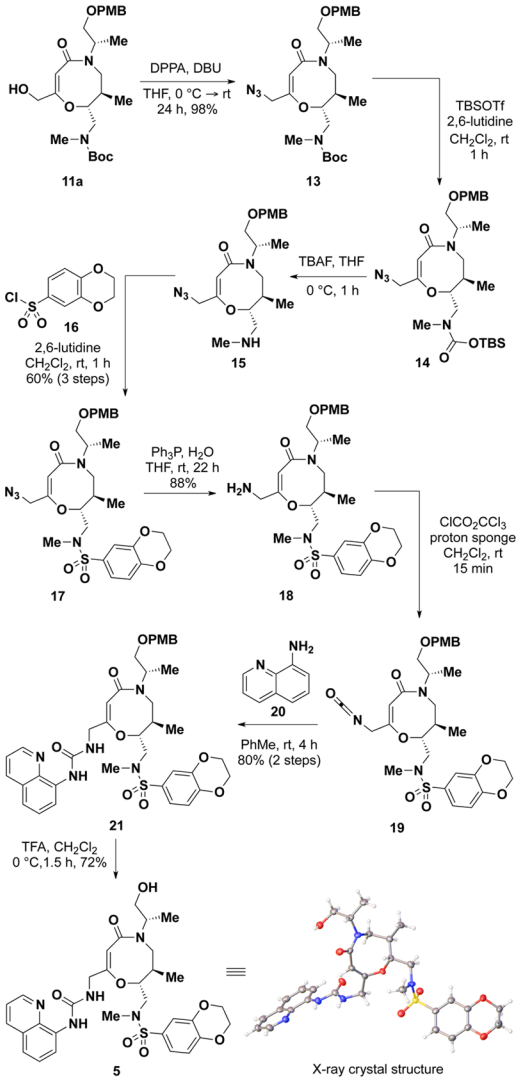
Scheme 4. Proposed Bidentate Coordination of Au(I)-Catalyst



Additionally, bidendate coordination[18] with the alkyne may provide activated species **A**. This mode of coordination may polarize the alkyne in a manner to favor cyclization of the alcohol to provide 8-*endo*-dig adduct **B**. The findings that propargyl alcohol **8b** does not afford oxazepanone products whereas TBS-protected congener **8c** and complex alkynamide **8a** do suggest that the 8-*endo* and 7-*exo* reaction pathways are not influenced by coordination of the propargylic alcohol of alkynamides with the gold(I) complex. The oxazepanone byproducts more likely arise from steric interactions imparted by substituents appended to the product heterocycles. After cyclization to intermediate **B**, protodeauration would then provide oxazocenones **11** with regeneration of the gold(I) catalyst.

Having developed a method to access oxazocenones, we next assessed the ability of oxazocenone **11a** to be elaborated to des-benzo analog **5** (Scheme 5). A synthesis of **5** was initiated by conversion of the primary alcohol of **11a** to an azide using

Scheme 5. Synthesis of Des-Benzo Quinoline Analog 5



diphenylphosphoryl azide (DPPA) to afford **13** in excellent yield (98%). The incorporated azide masks a primary amine needed to install the requisite urea moiety. Prior to urea formation, **13** was converted to sulfonamide **17** in three steps. To circumvent nonselective deprotection of the *p*-methoxybenzyl (PMB) ether under acidic conditions, the Boc-carbamate was cleaved by first subjecting **13** to *tert*-butyldimethylsilyl triflate (TBSOTF) to provide *N*-silylcarbamate **14**, which was then desilylated (TBAF) with decarboxylation to secondary crude amine **15**.[19] Subsequent capping with 1,4-benzodioxan-6-sulfonyl chloride **16** gave sulfonamide **17**. Staudinger reduction (Ph_3P, H_2O) of **17** to primary amine **18**, followed by treatment with diphosgene ($ClCO_2CCl_3$), afforded isocyanate **19**. This intermediate serves as a branching point to various urea derivatives, whereas, in this work, addition of 8-aminoquinoline **20** yielded PMB-protected des-benzo congener **21** in 80% yield from **18** in two steps. Deprotection of the PMB ether under oxidative conditions (e.g., DDQ) gave low yields of des-benzo congener **5**, in which byproducts resulting from allylic oxidation were observed.[20] Alternatively, acid-mediated cleavage of the PMB ether with trifluoroacetic acid (TFA) proceeded efficiently (72% yield) to complete the synthesis of **5**. The structure of **5** was assigned using X-ray crystallographic structure determination.

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In summary, we have described the development of a gold(I)-catalyzed 8-*endo*-dig hydroalkoxylation of alkynamides to form oxazocenones. This novel method was applied to a substrate with high structural complexity to obtain **5**, a des-benzo analog of a previously described bioactive benzoxazocenone generated by diversity-oriented synthesis. Biological evaluation of **5** is underway, and we are currently investigating the application of the optimized gold(I)-catalyzed conditions to access additional heterocyclic scaffolds.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures, compound characterization, X-ray crystal structures, and CIF data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Chou, D. H-C.; Duvall, J. R.; Gerard, B.; Liu, H.; Pandya, B. A.; Suh, B.-C.; Forbeck, E. M.; Faloon, P.; Wagner, B. K.; Marcaurelle, L. A. *ACS Med. Chem. Lett.* **2011**, *2*, 698. (b) Scully, S. S.; Tang, A. J.; Lundh, M.; Mosher, C. M.; Perkins, K. M.; Wagner, B. K. *J. Med. Chem.* **2013**, *56*, 4125. (c) Schaefer, G. I.; Perez, J. R.; Duvall, J. R.; Stanton, B. Z.; Shamji, A. F.; Schreiber, S. L. *J. Am. Chem. Soc.* **2013**, *135*, 9675. (d) Dandapani, S.; Germain, A. R.; Jewett, I.; le Quement, S.; Marie, J.-C.; Muncipinto, G.; Duvall, J. R.; Carmody, L. C.; Perez, J. R.; Engel, J. C.; Gut, J.; Kellar, D.; Siqueira-Neto, J. L.; McKerrow, J. H.; Kaiser, M.; Rodriguez, A.; Palmer, M. A.; Foley, M.; Schreiber, S. L.; Munoz, B. *ACS Med. Chem. Lett.* **2014**, *5*, 149.

(2) For selected reviews on diversity-oriented synthesis, see: (a) Schreiber, S. L. *Science* **2000**, *287*, 1964. (b) Burke, M. D.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 46. (c) Nielsen, T. E.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 48. (d) Galloway, W. R. J. D.; Isidro-Llobet, A.; Spring, D. R. *Nat. Commun.* **2010**, *1*, 80.

(3) For the preparation of benzoxazocenone scaffolds using diversity-oriented synthesis, see: Marcaurelle, L. A.; Comer, E.; Dandapani, S.; Duvall, J. R.; Gerard, B.; Kesavan, S.; Lee, M. D.; Liu, H.; Lowe, J. T.; Marie, J.-C.; Mulrooney, C. A.; Pandya, B. A.; Rowley, A.; Ryba, T. D.; Suh, B.-C.; Wei, J.; Young, D. W.; Akella, L. B.; Ross, N. T.; Zhang, Y.-L.; Fass, D. M.; Reis, S. A.; Zhao, W.-N.; Haggarty, S. J.; Palmer, M.; Foley, M. A. *J. Am. Chem. Soc.* **2010**, *132*, 16962.

(4) For base-mediated 8-*endo*-dig cyclization reactions of alcohols adding to ynones, see: (a) Schreiber, S. L.; Kelly, S. E. *Tetrahedron Lett.* **1984**, *25*, 1757. (b) Schreiber, S. L.; Kelly, S. E.; Porco, J. A., Jr.; Sammakia, T.; Suh, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 6210. (c) Rosas, N.; Sharma, P.; Alvarez, C.; Gómez, E.; Gutiérrez, Y.; Méndez, M.; Toscano, R. A.; Maldonado, L. A. *Tetrahedron Lett.* **2003**, *44*, 8019. (d) Matsuo, J.; Sasaki, S.; Hoshikawa, T.; Ishibashi, H. *Tetrahedron* **2008**, *64*, 11224.

(5) For palladium-mediated 8-*endo*-dig hydroalkoxylation reactions, see: (a) Davion, Y.; Guillaumet, G.; Léger, J.-M.; Jarry, C.; Lesur, B.; Mérour, J.-Y. *Heterocycles* **2003**, *60*, 1793. (b) Yoshimitsu, Y.; Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett.* **2013**, *15*, 3046.

(6) Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* **1981**, *14*, 95.

(7) For selected reviews on gold-catalyzed reactions, see: (a) Shapiro, N. D.; Toste, F. D. *Synlett* **2010**, 675. (b) Corma, A.; Leyva-Pérez, A.; Sabater, M. J. *Chem. Rev.* **2011**, *111*, 1657. (c) Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2012**, *41*, 2448. (d) Zhang, Y.; Luo, T.; Yang, Z. *Nat. Prod. Rep.* **2014**, *31*, 489.

(8) (a) Ferrer, C.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 1105. (b) Ferrer, C.; Amijs, C. H. M.; Echavarren, A. M. *Chem.—Eur. J.* **2007**, *13*, 1358. (c) Ferrer, C.; Escribano-Cuesta, A.; Echavarren, A. M. *Tetrahedron* **2009**, *65*, 9015.

(9) Wittstein, K.; Kumar, K.; Waldmann, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 9076.

(10) For examples of gold-catalyzed hydroalkoxylation reactions of alkynes, see: (a) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1415. (b) Liu, Y.; Song, F.; Song, Z.; Liu, M.; Yan, B. *Org. Lett.* **2005**, *7*, 5409. (c) Belting, V.; Krause, N. *Org. Lett.* **2006**, *8*, 4489. (d) Trost, B. M.; Dong, G. *Nature* **2008**, *456*, 485. (e) Diéguez-Vázquez, A.; Tzschucke, C. C.; Crecente-Campo, J.; McGrath, S.; Ley, S. V. *Eur. J. Org. Chem.* **2009**, 1698. (f) Chary, B. C.; Kim, S. *J. Org. Chem.* **2010**, *75*, 7928. (g) Corma, A.; Ruiz, V. R.; Leyva-Pérez, A.; Sabater, M. J. *Adv. Synth. Catal.* **2010**, *352*, 1701. (h) Fortner, K. C.; Kato, D.; Tanaka, Y.; Shair, M. D. *J. Am. Chem. Soc.* **2010**, *132*, 275. (i) Murai, M.; Uenishi, J.; Uemura, M. *Org. Lett.* **2010**, *12*, 4788. (j) Bihelovic, F.; Saicic, R. N. *Angew. Chem., Int. Ed.* **2012**, *51*, 5687. (k) Peshkov, V. A.; Pereshivko, O. P.; Van der Eycken, E. V. *Adv. Synth. Catal.* **2012**, *354*, 2841. (l) Brewitz, L.; Llaveria, J.; Yada, A.; Fürstner, A. *Chem.—Eur. J.* **2013**, *19*, 4532.

(11) Tsou, H.-R.; Mamuya, N.; Johnson, B. D.; Reich, M. F.; Gruber, B. C.; Ye, F.; Nilakantan, R.; Shen, R.; Discafani, C.; DeBlanc, R.; Davis, R.; Koehn, F. E.; Greenberger, L. M.; Wang, Y.-F.; Wissner, A. *J. Med. Chem.* **2001**, *44*, 2719.

(12) For analogous 6-*endo*-dig hydroalkoxylation reactions catalyzed by $(C_6F_5)_3PAuCl/AgOTf$, see: Kang, D.; Park, S.; Ryu, T.; Lee, P. L. *Org. Lett.* **2012**, *14*, 3912.

(13) For analogous AgOTf-catalyzed 6-*endo*-dig hydroalkoxylations of ynones, see: (a) Wang, C.; Forsyth, C. J. *Org. Lett.* **2006**, *8*, 2997. (b) Nicolaou, K. C.; Frederick, M. O.; Burtoloso, A. C. B.; Denton, R. M.; Rivas, F.; Cole, K. P.; Aversa, R. J.; Gibe, R.; Umezawa, T.; Suzuki, T. *J. Am. Chem. Soc.* **2008**, *130*, 7466. (c) Nicolaou, K. C.; Aversa, R. J.; Jin, J.; Rivas, F. *J. Am. Chem. Soc.* **2010**, *132*, 6855. (d) Fuwa, H.; Matsukida, S.; Sasaki, M. *Synlett* **2010**, 1239.

(14) An 80% yield for **11a** could be achieved when the catalyst loading for AgOTf was increased to 20 mol %.

(15) Dang, T. T.; Boeck, F.; Hintermann, L. *J. Org. Chem.* **2011**, *76*, 9353.

(16) Galli, C.; Giovannelli, G.; Illuminati, G.; Mandolini, L. *J. Org. Chem.* **1979**, *44*, 1258.

(17) Yamamoto, Y. *J. Org. Chem.* **2007**, *72*, 7817.

(18) (a) Blanc, A.; Tenbrink, K.; Weibel, J.-M.; Pale, P. *J. Org. Chem.* **2009**, *74*, 5342. (b) Lopez, S. S.; Engel, D. A.; Dudley, G. B. *Synlett* **2007**, 949−953. (c) Egi, M.; Azechi, K.; Saneto, M.; Shimizu, K.; Akai, S. *J. Org. Chem.* **2010**, *75*, 2123. (d) Hoffmann, M.; Weibel, J.-M.; de Frémont, P.; Pale, P.; Blanc, A. *Org. Lett.* **2014**, *16*, 908.

(19) Sakaitani, M.; Ohfune, Y. *J. Org. Chem.* **1990**, *55*, 870.

(20) Ronan, B.; Bacqué, E.; Barrière, J.-C.; Sablé, S. *Tetrahedron* **2003**, *59*, 2929.

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Org. Lett. 2015, 17, 418−421